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Committee of Experts on the Transport of Dangerous Goods and on the Globally Harmonized System of Classification and Labelling of Chemicals

Sub-Committee of Experts on the Transport of Dangerous Goods

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Item 3 of the provisional agenda
Listing, classification and packing

Toxicity of UN 2248, 2264 and 2357

Submitted by the expert from the Republic of Korea*

Introduction

1. At the forty-seventh session of the Sub-Committee, the Republic of Korea suggested that the hazardous information from the revised hazard profiles established by the Joint Group of Experts on the Scientific Aspects of Marine Environmental Protection (GESAMP) (PPR.1/Circ.1, Annex 5) could be useful data for identifying toxicity and corrosivity of some dangerous goods (ST/SG/AC.10/C.3/2015/11).

2. Some experts commented that detailed test data should be provided, as the hazardous reclassification of these substances may have a significant impact on the transport of dangerous goods. Accordingly, the Sub-Committee requested the submission of such information as required by the form in Figure 1 of the Recommendations (see ST/SG/AC.10/C.3/94 paras 35-37).

3. In this regard, the Republic of Korea collected test data on three substances that were recognized as necessary to reflect toxicity through a comparison between their GESAMP hazard profiles and their classification in the Dangerous Goods List of the Model Regulations. Based on the test data, amendments were proposed to the toxicity classification for the three substances (UN 2248, 2264 and 2357) during the forty-ninth and the fiftieth sessions (see informal document INF.33 and ST/SG/AC.10/C.3/2016/64). The outcome of the discussions is reflected in the report of the Sub-Committee on its fiftieth session (ST/SG/AC.10/C.3/100, paragraph 22), as follows:

> *"22. The Sub-Committee noted that the data provided by the Republic of Korea needed further consideration. It also noted that substances belonging to Class 8, packing group Ⅱ and, because of their inhalation toxicity, to Division 6.1, packing group Ⅱ, should be classified in Division 6.1 rather than Class 8. Some experts also thought that it would be important to check thoroughly whether the proposed changes in classification would not imply changes in conditions of transport."*.

* 2020 (A/74/6 (Sect.20) and Supplementary, Subprogramme 2.

Background

4. At the eighteenth session of the IMO Sub-Committee on Dangerous Goods, Solids Cargoes and Containers (DSC 18, 2013), the Republic of Korea made a proposal on marine pollutant information on the Dangerous Goods List in the IMDG Code concerning the substances meeting the criteria for environmentally hazardous substances according to the GESAMP hazard profiles (DSC 18/7/8).

5. The proposal was made to provide correct information for shippers and carriers. The IMO DSC Sub-Committee agreed to the proposal and these substances were identified as marine pollutants in the IMDG Code (Amendment 37-14) after verification of the Editorial & Technical Group of the Sub-Committee on the Carriage of Cargoes and Containers (E&T 20).

6. Similarly, assuming that the GESAMP hazard evaluation criteria and the classification for oral and dermal toxicity of the Model Regulations follow the same GHS criteria, the information on oral and dermal toxicity of the substances in the GESAMP hazard profiles could be valuable data to determine the hazard of substances listed in the Dangerous Goods List of the Model Regulations.

7. The grouping criteria of Division 6.1 for oral and dermal toxicity in the Model Regulations are the same as the criteria in the GESAMP hazard evaluation procedure (GESAMP Revised Reports and Studies No. 102). The grouping criteria for the oral toxicity (LD_{50}) and dermal toxicity (LD_{50}) are shown in C1 and C2 of table 1 according to the revised GESAMP hazard evaluation procedure. The grouping criteria for toxic substances in 2.6.2.2.4.1 of the Model Regulations are shown in table 2.

Table 1: Revised GESAMP Hazard evaluation procedure- Acute mammalian toxicity

	C Acute mammalian toxicity				
Numerical rating	C1 Oral toxicity	C2 Dermal toxicity	C3 Inhalation toxicity		
			C3a		C3b
			vapour/mist	mist only	vapour only
	LD_{50}/ATE (mg/kg)	LD_{50}/ATE (mg/kg)	LC_{50}/ATE (mg/l)	LC_{50}/ATE (mg/l)	LC_{50}/ATE (mg/l)
0	ATE > 2000	ATE > 2000	ATE > 20	ATE > 5	ATE > 20
1	300 < ATE ⩽ 2000	1000 < ATE ⩽ 2000	10 < ATE ⩽ 20	1 < ATE ⩽ 5	10 < ATE ⩽ 20
2	50 < ATE ⩽ 300	200 < ATE ⩽ 1000	2 < ATE ⩽ 10	0.5 < ATE ⩽ 1	2 < ATE ⩽ 10
3	5 < ATE ⩽ 50	50 < ATE ⩽ 200	0.5 < ATE ⩽ 2	0.05 < ATE ⩽ 0.5	0.5 < ATE ⩽ 2
4	ATE ⩽ 5	ATE ⩽ 50	ATE ⩽ 0.5	ATE ⩽ 0.05	ATE ⩽ 0.5

* In the table, ***ATE*** means "*Acute Toxicity Estimate"*.

Table 2: Grouping criteria for toxic substances in the Model Regulations

Packing Group	Oral toxicity LD_{50} (mg/kg)	Dermal toxicity LD_{50} (mg/kg)	Inhalation toxicity by dusts and mists LC_{50} (mg/l)
I	≤ 5.0	≤ 50	≤ 0.2
II	> 5.0 and ≤ 50	> 50 and ≤ 200	> 0.2 and ≤ 2.0
III	> 50 and ≤ 300	> 200 and ≤ 1000	> 2.0 and ≤ 4.0

8. Following the GESAMP hazard profiles, substances meeting numerical rating 2 and over in column C1 and C2 of table 1 which are not classified in Division 6.1 of the Model Regulations could be considered as potential toxic substances according to the criteria in 2.6.2.2.4.1 of the Model Regulations, as shown in table 3 below.

Table 3: Comparison of the grouping criteria of the toxic substances in the GESAMP hazard evaluation procedure and in the Model Regulations

Model Regulations	Oral toxicity LD50 (mg/kg)	Dermal toxicity LD50 (mg/kg)	GESAMP hazard profiles
Packing Group			Numerical rating
I	≤ 5.0	≤ 50	4
II	> 5.0 and ≤ 50	> 50 and ≤ 200	3
III	> 50 and ≤ 300	> 200 and ≤ 1000	2

9. The Republic of Korea believes that the hazardous classification of substances according to the Model Regulations has a significant impact on the safe transport, and therefore hazardous information should be reflected based on the most up-to-date and reliable data.

10. Through comparison with the dangerous goods list and the GESAMP hazard profiles, three substances were identified as having a toxicity or a recognized hazard from a number of test results among the substances with different toxicological information submitted to the GESAMP hazard profile and the hazard information registered in the Model Regulations. These three substances are listed in table 4 below.

Table 4: List of substances which could be classified as Division 6.1

Dangerous Goods List in the Model Regulations			GESAMP hazard profiles		
UN No.	Class	Proper shipping name	EHS name	C1	C2
2248	8 (3)	DI-n-BUTYLAMINE	Di-n-butylamine	2	2
2264	8 (3)	N,N-DIMETHYL-CYCLOHEXYLAMINE	N,N-Dimethyl cyclohexylamine	1	2
2357	8 (3)	CYCLOHEXYLAMINE	Cyclohexylamine	2	2

11. GESAMP is a group of experts belonging to IMO (International Maritime Organization) and other international organizations which is building hazard data on hazardous substances to protect the marine environment.

12. The Republic of Korea submits, together with annex I, detailed data on the toxicity of UN 2248, 2264 and 2357. Annex I provides a general overview of the acute toxicity data of these three substances as well as explanations why specific data were used as a basis for the proposed amendments.

13. Therefore, we propose amendments to the classification of UN 2248, 2264 and 2357 as indicated below, taking account of the data provided and the opinions expressed by transport of dangerous goods experts during the previous discussions.

Amendments to UN 2248

Rationale

14. Based on the data provided (for details, refer to Annex II), UN 2248 has an oral toxicity (LD_{50}) of 220mg/kg and a dermal toxicity (LD_{50}) of 768 mg/kg.

15. The inhalation toxicity value for vapours is 218 ppm (4h exposure). The Model Regulations specifies that LC_{50} values should be based on 1h exposure. Therefore, this value should be converted to 436 ppm on 1h exposure by multiplying the LC_{50} (4h value) by 2 for vapours (see 2.6.2.2.4.5 of the Model Regulations). Since the value refers to inhalation toxicity for vapours, the packing group should be calculated with the saturated vapour concentration (hereafter SVC) in accordance with 2.6.2.2.4.3 of the Model Regulations. The SVC was calculated using the equation included in the report from the National Institute for

Public Health and the Environment of the Netherlands (RIVM) circulated as informal document INF.8 for the thirty-third session of the Sub-Committee[1]:

$$SVC\ (ml/m^3) = VP/(R \times T) \times v_m \times 1000$$

Where: VP is the vapour pressure at 20°C (Pa)

R is the gas constant (8.314 m^3 Pa/K mole)

T is the temperature (at 293 K, equals 20°C)

v_m is the molar volume of ideal gas (24.1 l/mol at 20°C)

1000 is the conversion factor between ml and l (1000 ml/l)

16. The vapour pressure of the Di-n-butylamine was confirmed as 0.27 kPa (=270 Pa) at 20 ° C. This value was taken from the ILO International Chemical Safety Cards (https://pubchem.ncbi.nlm.nih.gov/compound/8148#section=Vapor-Pressure).

17. According to the results of the calculation, the SVC of the Di-n-butylamine is 2671 ml/m^3.

18. In conclusion, the LC_{50} of UN 2248 is 436 ppm for 1h exposure as mentioned above, with the units ml/m^3 deemed to be equivalent to ppm.

19. The Model Regulations stipulate in paragraph 2.6.2.2.4.3 (b), that liquids having toxic vapours shall be assigned to packing group II if SVC $\geqslant$ LC_{50} and LC_{50} $\leqslant$ 3000 ml/m^3 and not meeting the criteria for packing group I in 2.6.2.2.4.3 (a).

20. Although only acute oral and dermal toxicity were considered to evaluate the toxicity by comparison with the GESAMP hazard profiles in the early stage of the amendment, the inhalation toxicity should be considered in the proposal for proper classification of UN 2248.

21. Therefore, UN 2248 should be classified in Division 6.1, packing group II.

22. Accordingly, the primary hazard of UN 2248 should be changed to division 6.1 and class 8 should be added as a subsidiary hazard in accordance with the table of precedence of hazards in 2.0.3.3 of the Model Regulations.

23. Also, the limited (LQ) and exempted quantities (EQ) codes and the tank instructions should be revised in accordance with the Guiding Principles, following the revision of the major hazard. There is no need to change any other transport conditions such as the packing instructions.

Proposal

24. Amend the entry for UN 2248 in the Dangerous Goods list as follows (new text is shown in **red, bold, underlined**, deleted text is ~~crossed-out~~):

UN No.	Name and description	Class or division	Sub-sidiary hazard	UN packing group	Special provi-sions	Limited and excepted quantities		Packagings and IBCs		Portable tanks and bulk containers	
								Packing instruction	Special packing provisions	Instruc-tions	Special provisions
(1)	(2)	(3)	(4)	(5)	(6)	(7a)	(7b)	(8)	(9)	(10)	(11)
2248	DI-n-BUTYLAMINE	~~8~~ **6.1**	3 **8**	II	-	~~1L~~ **100ml**	~~E2~~ **E4**	P001 IBC02	-	~~T7~~ **T20**	TP2 **TP13**

[1] http://www.unece.org/fileadmin/DAM/trans/doc/2008/ac10c3/UN-SCETDG-33-INF08e.pdf.

Amendments to UN 2264

Rationale

25. Based on the data provided (for details, refer to Annex III), the toxicity of UN 2264 is determined by an oral toxicity (LD_{50}) of 272 mg/kg and an acute dermal toxicity (LD_{50}) of 380 mg/kg.

26. Therefore, according to Table 2, UN 2264 should be classified in Division 6.1, packing group III.

27. The primary hazard of UN 2264 should remain as class 8 and division 6.1 should be added as subsidiary hazard according to the table of precedence of hazards in 2.0.3.3 of the Model Regulations.

28. There is no need to change any other transport conditions such as the packing instructions, or the limited (LQ) or exempted quantities (EQ), as we confirmed.

29. The inhalation toxicity value for vapours is between 1.7 – 5.8 mg/l (320 ppm to 1120 ppm) for 6h exposures. There is no method in the Model Regulations to use 6h exposure for a 1h exposure limit. If we could arbitrarily apply the conversion method for vapours by analogy to the 4h exposure conversion method, of 2 multiplied by 3 to the 6h exposure, this data could be converted to 5.1 – 17.4 mg/l related to 1h exposure. But the range of this value is too broad and taking into account that, as mentioned above, there is no stipulated method for converting the value for 6h exposure to a 1h exposure, the inhalation toxicity of UN 2264 has not been taken into account in the proposal.

Proposal

30. Amend the entry for UN 2264 in the list of dangerous goods as follows (new text is shown in **red, bold, underlined**):

UN No.	Name and description	Class or division	Subsi-diary hazard	UN packing group	Special provi-sion	Limited and excepted quantities		Packagings and IBCs		Portable tanks and bulk containers	
								Packing instruction	Special packing provisions	Instruc-tions	Special provisions
(1)	(2)	(3)	(4)	(5)	(6)	(7a)	(7b)	(8)	(9)	(10)	(11)
2264	N,N-DIMETHYL-CYCLOHEXYLAMINE	8	3 **6.1**	II	-	1L	E2	P001 IBC02	-	T7	TP2

Amendments to UN 2357

Rationale

31. Based on the data provided (for details, please refer to Annex IV), UN 2357 has an oral toxicity (LD_{50}) of 156 mg/kg and an acute dermal toxicity (LD_{50}) of 631-1000 mg/kg.

32. Therefore, according to the Table 2, UN 2357 should be classified in Division 6.1, packing group III.

33. The primary hazard of UN 2357 should remain as class 8, and division 6.1 should be added as a subsidiary hazard according to the table of precedence of hazards in 2.0.3.3 of the Model Regulations.

34. There is no need to change any other transport conditions such as the packing instructions, the limited (LQ) or exempted quantities (EQ).

Proposal

35. Amend the entry for UN 2357 in the Dangerous Goods List as follows (new text is shown in **red, bold, underlined**):

UN No.	Name and description	Class or division	Subsi-diary hazard	UN packing group	Special provi-sion	Limited and excepted quantities		Packagings and IBCs		Portable tanks and bulk containers	
								Packing instruction	Special packing provisions	Instruc-tions	Special provisions
(1)	(2)	(3)	(4)	(5)	(6)	(7a)	(7b)	(8)	(9)	(10)	(11)
2357	CYCLOHEXYLAMINE	8	3 **6.1**	II	-	1L	E2	P001 IBC02	-	T7	TP2

Annex I [English only]

Data overview

UN 2248, Di-n-butylamine CAS No. 111-92-2						
Acute toxicity	Reference type	GLP Compliance	*Reliability	Result	GHS	Link
oral	Study report	No	2*	LD_{50} (rat) 550 mg/kg bw 95% CL: 480 - 620	Cat.4	https://echa.europa.eu/sv/registration-dossier/-/registered-dossier/13527/7/3/2
	Publication (Revista de Chimie, 36(667), 1985)			LD_{50} (rat) 189 mg/kg bw	Cat.3	https://pubchem.ncbi.nlm.nih.gov/compound/8148#section=NIOSH-Toxicity-Data&fullscreen=true
	Publication (Gigiena i Sanitariya. For English translation, see HYSAAV., 40(11)(21), 1975)			LD_{50} (mouse) 290 mg/kg	Cat. 3	https://pubchem.ncbi.nlm.nih.gov/compound/8148#section=Acute-Effects&fullscreen=true
	Publication (Gigiena i Sanitariya. For English translation, see HYSAAV., 40(11)(21), 1975)			LD_{50} (guinea pig) 230 mg/kg	Cat. 3	https://pubchem.ncbi.nlm.nih.gov/compound/8149#section=Acute-Effects&fullscreen=true
	Publication (Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996., p. 1069)	-	-	LD_{50} Rat oral 220 mg/kg	Cat. 3	https://pubchem.ncbi.nlm.nih.gov/source/hsdb/310#section=Non-Human-Toxicity-Values&fullscreen=true
	Publication (Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996., p. 1069)			LD_{50} Mouse oral 290 mg/kg	Cat. 3	https://pubchem.ncbi.nlm.nih.gov/source/hsdb/310#section=Non-Human-Toxicity-Values&fullscreen=true
	Publication (Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3.			LD_{50} Guinea pig oral 230 mg/kg	Cat. 3	https://pubchem.ncbi.nlm.nih.gov/source/hsdb/310#section=Non-Human-Toxicity-Values&fullscreen=true

UN 2248, Di-n-butylamine CAS No. 111-92-2						
Acute toxicity	Reference type	GLP Compliance	*Reliability	Result	GHS	Link
	New York, NY: Van Nostrand Reinhold, 1996., p. 1069)					
	- Studies on the acute oral toxicity of Dibutylamine are available in a number of bibliographic data. - The acute oral toxicity of UN 2248 is cited in EU REACH registration data with only one test report (#1) conducted in 1950, and it's submitted by Cat.4. - The pattern of acute toxicity of Dibutylamine in the data examined outside the EU REACH registration data was found in Cat.3, and the cited literature was cited frequently in the US EPA HSDB, etc. and judged to have the same reliability as the test data used in the EU REACH registration data. - Provided that the examined data are equally reliable, many of the data are assigned as GHS Cat.3 and the worst value is also assigned as GHS Cat.3. - Consequently, the acute oral toxicity value corresponds to GHS Cat.3 which corresponds to the classification criteria of PG III for Division 6.1.					
Dermal	Study report	No	2	LD_{50} (rabbit, 24h) 768 mg/kg bw 95% CL: 620 – 1,130	Cat.3	https://echa.europa.eu/sv/registration-dossier/-/registered-dossier/13527/7/3/4
	Publication (National Technical Information Service., OTS0535430)			LD_{50} (rabbit) 770 mg/kg	Cat.3	https://pubchem.ncbi.nlm.nih.gov/compound/8148#section=Acute-Effects&fullscreen=true
	Publication (Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996., p. 1069)			LD_{50} (rabbit) 1010 mg/kg	Cat.4	https://pubchem.ncbi.nlm.nih.gov/compound/8148#section=Non-Human-Toxicity-Values&fullscreen=true
	- Three studies on the acute dermal toxicity of Dibutylamine are available. - In the EU REACH registration data, only one test report carried out in 1951 is cited, representing GHS Cat.3. - In other literature, the acute dermal toxicity value of Dibutylamine was confirmed as GHS Cat.3 and 4 respectively. - One test report and two literature were all considered to have the same reliability, and Dibutylamine was judged to be assigned as GHS Cat.3 citing the worst value which corresponds to classification criteria of PG III for Division 6.1.					

UN 2248, Di-n-butylamine CAS No. 111-92-2						
Acute toxicity	Reference type	GLP Compliance	*Reliability	Result	GHS	Link
Inhalation	Study report	Yes	2	LC_{50} (4h, rat) 218 ppm (= 1.15 mg/l)	Cat.2	https://echa.europa.eu/sv/registration-dossier/-/registered-dossier/13527/7/3/3
	Study report	No	2	LC_{50} (4h, rat) > 1.34 - < 2.68 mg/l	Cat.2	https://echa.europa.eu/sv/registration-dossier/-/registered-dossier/13527/7/3/3/?documentUUID=022335f9-857a-4952-a1c6-f5e8e88255df
	- Three studies on the acute inhalation toxicity of Dibutylamine are available. - The EU REACH cites test data carried out in 1951, 1952 and 1987. Test data in 1987, which was carried out recently, has been submitted as key data and was evaluated as Cat.2. - Therefore, the acute inhalation toxicity of Dibutylamine is considered to be assigned as Cat.2.					

*: R*eliable with restrictions, according to ECHA*

UN 2264, N,N-Dimethyl cyclohexylamine CAS no. 98-94-2						
Acute toxicity	Reference type	GLP compliance	Reliability	result	GHS	Link
oral	Study report	No	2	272 mg/kg < LD_{50} (rat) < 289 mg/kg bw	Cat.3	https://echa.europa.eu/registration-dossier/-/registered-dossier/13521/7/3/2
	Study report			LD50 = 337 mg/kg(240-472) (rat) 283 mg/kg(188-426) (mouse)	Cat. 3	Health, Safety, and Human Factors Laboratory, Eastman Kodak Company **(Refer to attached report p.17)**
	Publication			LD_{50}=520 mg/kg (guinea pig)	Cat. 4	https://pubchem.ncbi.nlm.nih.gov/compound/7415#section=NIOSH-Toxicity-Data&fullscreen=true
	Publication			LD_{50}=320 mg/kg (mouse)	Cat. 4	https://pubchem.ncbi.nlm.nih.gov/compound/7415#section=NIOSH-Toxicity-Data&fullscreen=true
	Publication			LD_{50}=620 mg/kg (rabbit)	Cat. 4	https://pubchem.ncbi.nlm.nih.gov/compound/7415#section=NIOSH-Toxicity-Data&fullscreen=true
	Publication			LD_{50}=348 mg/kg (rat)	Cat. 4	https://pubchem.ncbi.nlm.nih.gov/compound/7415#section=NIOSH-Toxicity-Data&fullscreen=true
	- Highly reliable studies on acute oral toxicity of N.N-Dimethyl cyclohexylamine are very limited. - The EU REACH registration data only cites one test report conducted in 1979 and represents GHS Cat.3. - Several data were available on other literature and NIOSH TOXICITY DATA, and all of the data were assigned as Cat.4. - Provided that the data is equally reliable, the acute oral toxicity of N,N-Dimethyl cyclohexylamine is considered to be assigned as GHS Cat.3 and therefore, it meets the classification criteria of PGⅢ for Division 6.1, according to the worst data cited in SIDS Initial assessment profiles (https://hpvchemicals.oecd.org/UI/handler.axd?id=ee5efcff-697d-48f7-ab7d-032356a83370).					

UN 2264, N,N-Dimethyl cyclohexylamine CAS no. 98-94-2						
Acute toxicity	Reference type	GLP compliance	Reliability	result	GHS	Link
Dermal	Study report	Yes	2	LD_{50} (rat) 380 mg/kg	Cat.3	https://echa.europa.eu/registration-dossier/-/registered-dossier/13521/7/3/4
	Study report	Yes	2	LD_{50} (rat) > 400 mg/kg	Not classified	https://echa.europa.eu/registration-dossier/-/registered-dossier/13521/7/3/4/?documentUUID=c63bdc9f-e4f3-41c7-a94e-fcdb1c56ecaa
	Study report	Yes	2	LD_{50} (rat) > 400 mg/kg	Not classified	https://echa.europa.eu/registration-dossier/-/registered-dossier/13521/7/3/4/?documentUUID=1d745de2-2814-4d76-a245-52d02a5be09a
	Publication			LD_{50} = 370 mg/kg	Cat.3	https://pubchem.ncbi.nlm.nih.gov/compound/7415#section=NIOSH-Toxicity-Data&fullscreen=true
	- Most studies of acute dermal toxicity of N.N-Dimethyl cyclohexylamine are available from the data tested in the 1980s and 1990s. - Two out of three data showed no lethal action, and the data of lethal action was used as a key data in the EU REACH registration. - In addition, a data was available on NIOSH TOXICITY DATA and it is assigned as Cat.3. - Provided that the data from EU REACH key data and NIOSH are equally reliable, the acute dermal toxicity of N.N-Dimethyl cyclohexylamine is considered to be assigned as GHS Cat.3, and therefore, it meets the classification criteria of PG III for Division 6.1.					
Inhalation	Study report	Yes	2	LC_{50} 1.7-5.8 mg/L (6h, rat) (= 320 ppm to 1120 ppm)	Cat.3	https://echa.europa.eu/registration-dossier/-/registered-dossier/13521/7/3/3
	Study report	No	2	LC_{50} = 9,000 mg/m^3	Cat.3	https://echa.europa.eu/registration-dossier/-/registered-dossier/13521/7/3/3/?documentUUID=3b895cb8-c1e2-442d-ba9b-ef103e53f24a

UN 2264, N,N-Dimethyl cyclohexylamine CAS no. 98-94-2						
Acute toxicity	Reference type	GLP compliance	Reliability	result	GHS	Link
	Study report	No	2	LC_{50} < 11,710 mg/m³ air (1H)	Cat.3	https://echa.europa.eu/sv/registration-dossier/-/registered-dossier/13521/7/3/3/?documentUUID=8b0dbaef-c4e3-443b-961d-77fdea82aa07
	Publication			LC_{50} = 1,100 mg/m^3(2H)	Cat. 2	https://pubchem.ncbi.nlm.nih.gov/compound/7415#section=NIOSH-Toxicity-Data&fullscreen=true
	Publication			LC_{50} = 1,889 mg/m^3(2H)	Cat. 2	https://pubchem.ncbi.nlm.nih.gov/compound/7415#section=NIOSH-Toxicity-Data&fullscreen=true
	- Most of the data on acute inhalation toxicity of N.N-Dimethyl cyclohexylamine can be obtained from data tested in the 1980s and 1990s. - In the EU REACH, a test report conducted in 1988 was cited as key data and represents GHS Cat.3. - Two other data were available on NIOSH TOXICITY DATA, which were assigned as Cat.2. - Based on the test report judged to be the most reliable (GLP, EU REACH key data), the acute inhalation toxicity of N.N-Dimethyl cyclohexylamine is considered to be assigned as GHS Cat.3.					

UN 2357, Cyclohexylamine CAS no. 108-91-8						
Acute Toxicity	Reference type	GLP Compliance	Reliability	result	GHS	Link
oral	Publication (Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996., p. 960)	-	-	LD_{50} (rat) 156 mg/kg bw	Cat.3	https://pubchem.ncbi.nlm.nih.gov/compound/Cyclohexylamine#section=Non-Human-Toxicity-Values&fullscreen=true
	Other (National Technical Information Service., OTS0534836)	-	-	LD_{50} (rat) 11 mg/kg bw	Cat.2	https://pubchem.ncbi.nlm.nih.gov/compound/Cyclohexylamine#section=NIOSH-Toxicity-Data&fullscreen=true https://echa.europa.eu/registration-dossier/-/registered-dossier/13348/7/3/2/?documentUUID=7db775d0-0a4b-40f3-862d-f8e33e24187c
	Publication	-	-	LD_{50} (rat) 530 mg/kg bw	Cat.4	https://pubchem.ncbi.nlm.nih.gov/compound/Cyclohexylamine
	Publication	-	-	LD_{50} (rat) 224 mg/kg bw	Cat.3	https://pubchem.ncbi.nlm.nih.gov/compound/Cyclohexylamine#section=NIOSH-Toxicity-Data&fullscreen=true
	Study report	No	2	LD_{50} (rat) 350 mg/kg bw	Cat.4	https://echa.europa.eu/documents/10162/3baf4dd8-ae8a-eca0-8e2a-d617a12fc29e
	Study report	No	2	Mortality : 0, 0, 0, 0, 2, 4, 9, 13, 15, 15/15 respectively at 25, 50, 100, 250, 300, 350, 500, 600, 750, 1000 mg/kg bw LD50 : 432 mg/kg bw (Read-across; CN 4998-76-9)	Cat.4	https://echa.europa.eu/documents/10162/3baf4dd8-ae8a-eca0-8e2a-d617a12fc29e

UN 2357, Cyclohexylamine CAS no. 108-91-8						
Acute Toxicity	Reference type	GLP Compliance	Reliability	result	GHS	Link
	- There is limited reliable data on the acute oral toxicity of Cyclohexylamine and most of the study results can be found from the literature studied a long time ago. - In a number of studies in the EU REACH registration data, acute oral toxicity of Cyclohexylamine has a range of 2~4 according to GHS. - The most reliable data(reliability 2) commonly showed Cat.4, and the acute oral toxicity of Cyclohexylamine in EU REACH registration was submitted by Cat.4 accordingly. - But the pattern of the acute oral toxicity of Cyclohexylamine in the data outside of EU REACH registration data also appeared in range of Cat. 2~ 4. - Among the various data, the data assigned as Cat.2 was excluded since it was very limited and not reliable. So the worst value was selected among the data considered to have the same reliability except Cat.2, acute oral toxicity of Cyclohexylamine is considered to be assigned as GHS Cat.3. Therefore, it meets the classification criteria of PG III for class 6.1.					
Dermal	Publication (Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996., p. 961)	-	-	LD_{50} (rabbit) 277 mg/kg	Cat.3	https://pubchem.ncbi.nlm.nih.gov/compound/Cyclohexylamine#section=Non-Human-Toxicity-Values&fullscreen=true
	Study report	No	4	LD_{50} 275 mg/kg	Cat.3	https://echa.europa.eu/registration-dossier/-/registered-dossier/13348/7/3/4/?documentUUID=f9bd1fe9-6918-4468-88ed-1cdb7a61382f
	Publication (The MAK-Collection Part I: MAK Value Documentations, Vol. 22. DFG, Deutsche Forschungsgemeinscha)	No	4	LD_{50} > 631 - < 1,000 mg/kg	Cat.3	https://echa.europa.eu/registration-dossier/-/registered-dossier/13348/7/3/4/?documentUUID=c8cc6b67-5607-45e4-87d3-1dc01649f75e
	- Three studies on the acute dermal toxicity of Cyclohexylamine are available. - All three represent GHS Cat.3, two of which are cited in the EU REACH registration dossier. - Judging from the weighting method of the evidence, acute dermal toxicity of Cyclohexylamine is considered to be assigned as GHS Cat.3, and therefore, it meets the classification criteria of PG III for class 6.1.					

UN 2357, Cyclohexylamine CAS no. 108-91-8						
Acute Toxicity	Reference type	GLP Compliance	Reliability	result	GHS	Link
Inhalation	No data					
	- The acute inhalation toxicity of Cyclohexylamine is considered to be low, and no reliable data can be identified from the survey data.					

※ Klimisch score

Score	Description	Details (quoted from paper)
1	Reliable without restriction	"This includes studies or data from the literature or reports which were carried out or generated according to generally valid and/or internationally accepted testing guidelines (preferably performed according to GLP) or in which the test parameters documented are based on a specific (national) testing guideline (preferably performed according to GLP) or in which all parameters described are closely related/comparable to a guideline method"
2	Reliable with restriction	"This includes studies or data from the literature, reports (mostly not performed according to GLP), in which the test parameters documented do not totally comply with the specific testing guideline, but are sufficient to accept the data or in which investigations are described which cannot be subsumed under a testing guideline, but which are nevertheless well documented and scientifically acceptable."
3	Not reliable	"This includes studies or data from the literature/reports in which there are interferences between the measuring system and the test substance or in which organisms/test systems were used which are not relevant in relation to the exposure (e.g., unphysiological pathways of application) or which were carried out or generated according to a method which is not acceptable, the documentation of which is not sufficient for an assessment and which is not convincing for an expert judgment."
4	Not assignable	"This includes studies or data from the literature, which do not give sufficient experimental details and which are only listed in short abstracts or secondary literature (books, reviews, etc.)."
Source: WIKIPEDIA(https://en.wikipedia.org/wiki/Klimisch_score)		

Annex II [English only]

Data sheet for Di-n-butylamine(UN 2248)[2]

Section 5. HARMFUL BIOLOGICAL EFFECTS

5.1 LD_{50}, oral (2.6.2.1.1[3]) ……**220** mg/kg[a] Animal species ……..**Rat**

5.2 LD_{50}, dermal (2.6.2.1.2) ……..….. **768** mg/kg[b] Animal species …….**Rabbit**

5.3 LC_{50}, inhalation (2.6.2.1.3) ……. **1.15** mg/l[c] Exposure time……..**4 hours**

or …**218** ml/m^3 Animal species ……..…..**Rat**

5.4 Saturated vapour concentration at 20℃ (2.6.2.2.4.3) ……...…**2670** ml/m^3

5.5 Skin exposure (2.8) results : **Corrosive**[d] Exposure time…**3 minutes and 1 hour**

Animal species……...…… **Rabbit**

5.6 Other data[e]

Corrosive, severe skin and eye irritant, reproductive toxicity, germ cell mutagenicity and specific target organ toxicity (single exposure)

Ecological toxicity

Fish (*Salmo gairdneri*), LC_{50} (96h) : 37mg/L[f]

Aquatic invertebrates (*Daphnia magna*), EC_{50} (48h) : 65.98mg/L[g]

5.7 Human experience……..…**not applicable**

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[2] References:

[a] Lewis, R.J., 1996, Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, p. 1069

[b] European Chemical Agency (ECHA), Dibutylamine - Registration Dossier (https://echa.europa.eu/registration-dossier/-/registered-dossier/13527/7/3/4)

[c] European Chemical Agency (ECHA), Dibutylamine - Registration Dossier (https://echa.europa.eu/registration-dossier/-/registered-dossier/13527/7/3/3)

[d] European Chemical Agency (ECHA), Dibutylamine - Registration Dossier (https://echa.europa.eu/registration-dossier/-/registered-dossier/13527/7/4/2)

[e] European Chemical Agency (ECHA), Dibutylamine - Registration Dossier (https://echa.europa.eu/registration-dossier/-/registered-dossier/13527/2/1)

[f] Calamari, D., et al., 1980, Estimating the hazard of eight amines on aquatic life. Chemosphere 9, 753

[g] European Chemical Agency (ECHA), Dibutylamine - Registration Dossier (https://echa.europa.eu/registration-dossier/-/registered-dossier/13527/6/2/4)

[3] This and similar references are to chapters and paragraphs in the Model Regulations on the Transport of Dangerous Goods.

Annex III [English only]

Data sheet for N, N-Dimethyl cyclohexylamine (UN 2264)[4]

Section 5. HARMFUL BIOLOGICAL EFFECTS

5.1 LD_{50}, oral (2.6.2.1.1[5]) ……**>272 - <289** mg/kg[a] Animal species ……..**Rat**

5.2 LD_{50}, dermal (2.6.2.1.2) ……..… **380** mg/kg[b] Animal species ……..**Rat**

5.3 LC_{50}, inhalation (2.6.2.1.3) …… 1.7-5.8 mg/L[c] Exposure time…..**6 hour**

or …….ml/m^3 Animal species ……..**Rat**

5.4 Saturated vapour concentration at 20℃ (2.6.2.2.4.3) ……..…**2860** ml/m^3

5.5 Skin exposure (2.8) results : **Corrosive**[d] Exposure time……..…….**No data**

Animal species……**Rabbit**

5.6 Other data[e]

Corrosive, severe skin and eye irritant, reproductive toxicity, germ cell mutagenicity, carcinogenicity and specific target organ toxicity (single and repeated exposure)

Ecological toxicity

Fish (*Oncorhynchus mykiss*), LC_{50} (96h) : 28mg/L[f]

Aquatic plants (*Scenedesmus subspicatus*), EC_{50} (72h) : 0.79mg/L[g]

5.7 Human experience……..….Not applicable

[4] References:
[a] European Chemical Agency (ECHA), Cyclohexyldimethylamine - Registration Dossier (https://echa.europa.eu/registration-dossier/-/registered-dossier/13521/7/3/2)
[b] European Chemical Agency (ECHA), Cyclohexyldimethylamine - Registration Dossier (https://echa.europa.eu/registration-dossier/-/registered-dossier/13521/7/3/4)
[c] European Chemical Agency (ECHA), Cyclohexyldimethylamine - Registration Dossier (https://echa.europa.eu/registration-dossier/-/registered-dossier/13521/7/3/3)
[d] European Chemical Agency (ECHA), Cyclohexyldimethylamine - Registration Dossier (https://echa.europa.eu/registration-dossier/-/registered-dossier/13521/7/4/2/?documentUUID=00a77466-5f8a-48a9-908c-39fb2a6053a5)
[e] European Chemical Agency (ECHA), Cyclohexyldimethylamine - Registration Dossier (https://echa.europa.eu/registration-dossier/-/registered-dossier/13521/2/1)
[f] European Chemical Agency (ECHA), Cyclohexyldimethylamine - Registration Dossier (https://echa.europa.eu/registration-dossier/-/registered-dossier/13521/6/2/2)
[g] European Chemical Agency (ECHA), Cyclohexyldimethylamine - Registration Dossier (https://echa.europa.eu/registration-dossier/-/registered-dossier/13521/6/2/6)

[5] This and similar references are to chapters and paragraphs in the Model Regulations on the Transport of Dangerous Goods.

Annex IV [English only]

Data sheet for Cyclohexylamine (UN 2357)[6]

Section 5. HARMFUL BIOLOGICAL EFFECTS

5.1 LD_{50}, oral (2.6.2.1.1[7]) ……**156** mg/kg[a] Animal species ……..**Rat**

5.2 LD_{50}, dermal (2.6.2.1.2) ……**>631 - <1000**mg/kg[b] Animal species ……..…**Rabbit**

5.3 LC_{50}, inhalation (2.6.2.1.3) …...no data…... mg/l Exposure time……..**no data**

or ……..….ml/m^3 Animal species …….

5.4 Saturated vapour concentration at 20℃ (2.6.2.2.4.3) ……**13800** ml/m^3

5.5 Skin exposure (2.8) results : **Corrosive**[c] Exposure time……**4** hours

Animal species……**Rabbit**

5.6 Other data[d]

Corrosive, severe skin and eye irritant, reproductive toxicity, germ cell mutagenicity, carcinogenicity and specific target organ toxicity (single and repeated exposure)

Ecological toxicity

Fish (*Oryzias latipes*), LC_{50} (96h) : 33mg/L[e]

Aquatic invertebrates (*Daphnia magna*), EC_{50} (24h) : 80mg/L[f]

5.7 Human experience……..……. Not applicable

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[6] References:
[a] Lewis, R.J., 1996, Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, p. 960
[b] European Chemical Agency (ECHA), CYCLOHEXYLAMINE - Registration Dossier (https://echa.europa.eu/registration-dossier/-/registered-dossier/13348/7/3/4/?documentUUID=c8cc6b67-5607-45e4-87d3-1dc01649f75e)
[c] European Chemical Agency (ECHA), CYCLOHEXYLAMINE - Registration Dossier (https://echa.europa.eu/de/registration-dossier/-/registered-dossier/13348/7/4/2/?documentUUID=d516cd27-1283-4151-9832-18a05a74b703)
[d] European Chemical Agency (ECHA), CYCLOHEXYLAMINE - Registration Dossier (https://echa.europa.eu/de/registration-dossier/-/registered-dossier/13348/2/1)
[e] European Chemical Agency (ECHA), CYCLOHEXYLAMINE - Registration Dossier (https://echa.europa.eu/de/registration-dossier/-/registered-dossier/13348/6/2/2)
[f] Bringmann G and Kuehn R, 1977, Befunde der Schadwirkung wassergefaehrdender Stoffe gegen Daphnia magna. Z. Wasser-Abwasser-Forsch. 10, 161

[7] This and similar references are to chapters and paragraphs in the Model Regulations on the Transport of Dangerous Goods.